KAISER PERMANENTE®

Review Criteria
Georgia Region

TITLE	**Proton Beam Therapy**	CRITERIA NUMBER	01-49
DEPARTMENT	QUALITY RESOURCE MANANGEMENT	EFFECTIVE DATE	7/17/2015
SECTION	UTILIZATION MANAGEMENT	REVIEW DATES	2/15/2016 2/12/2018
		REVISION DATE	2/11/2019 2/1/2020 7/17/2020 1/21/2021 1/20/2022 2/28/2023
TYPE	(X) New (X) Reviewed/Revised	PAGE NUMBER	Page 1 of 7

Purpose: This policy provides background information, expert opinions, and references on the use of Proton Beam therapy for the Quality Resource Management staff when they receive a request for this service.
All request for Proton Beam Therapy including Emory Proton Beam Center should be discussed with TSPMG Chief Radiation Oncology and Physician Director of Medical Specialities (currently John Strikler) .
Discussion and decision should be documented in Referral.
Most adult patients will need to be evaluated by internal Radiation Oncology prior to external referral.
DIAGNOSIS/CONDITION:
CPT-4/ HCPCS CODE AND DESCRIPTION: INDICATORS 77520; 77522; 77523; 77525

PBT is a type of radiotherapy using protons rather than the photons as in traditional external beam radiation therapy. PBT is used to treat solid tumors and is intended to minimize total radiation dose and side effects, including potential damage to surrounding healthy tissues. PBT can be used as monotherapy or in conjunction with other standard treatment strategies such as surgery, chemotherapy, and even conventional photon beam radiotherapy

1.0 INDICATIONS

1.1 Chordomas or chondrosarcomas arising at the base of the skull or cervical spine without distant metastases; *or*

1.2 Malignancies in children (21 years of age and younger); *or*

1.3 Uveal melanomas confined to the globe (i.e., not distant metastases) (the uvea is comprised of the iris, ciliary body, and choroid [the vascular middle coat of the eye]).

1.4 Secondary malignancies in the head and neck region for which the member has been previously treated with radiation therapy

2.0 Proton beam radiotherapy for treatment of prostate cancer is not medically necessary for individuals with localized prostate cancer because it has not been proven to be more effective than other radiotherapy modalities for this indication. Proton beam therapy for metastatic prostate cancer is considered experimental and investigational.

- Coverage currently limited to TTP or Multichoice members (using out of network benefit) since this procedure is as effective as standard XRT for prostate cancer.

2.0 VIEWS OF THE SOUTHEAST PERMANENTE MEDICAL GROUP

Based on current Southern California Kaiser Tech review and expert opinion from PMG Radiation Oncologists in Scal and Ga, Proton beam therapy (PBT) is as good as standard radiation therapy for localized prostate cancer including IMRT, and brachytherapy. Clinical studies are still underway to determine whether there is less morbidity associated with PBT. Since the evidence does not indicate that it is superior to standard radiation therapy for this indication, coverage for this indication is limited to TTP and Multichoice Members.

Proton Beam therapy may be indicated for pediatric patients, and adults with skull-based tumors but all requests should be discussed with and approved by the TSPMG Radiation Oncologist and Chief of Oncology since alternate therapy may be indicated. (see indications above). AMD approval is required as well

Expert Opinions:

Proton Beam Therapy - PMG Clinical Input (July 2, 2015)

1) TSPMG Radiation Oncologist, Ahmed Ali MD:

Dr. Ali reports that he has had good success with treating localized prostate cancer with standard radiation therapy and that PBT was not superior and not medically necessary.

2) Ricardo Wang, MD, Regional Chief and Chief of Service, Regional Radiation Oncology

Proton therapy is only one of the many ways we treat prostate cancer patients with radiation.
We can use IGRT, IMRT, Brachytherapy, etc.
No study has shown superiority of protons over other treatment modalities
There MAY be some decrease morbidity with protons, but this is currently being studied in randomized studies. There's absolutely no data which show increased survival with protons.

As Dr Schotinger stated, we've been upheld every time we've denied protons.

3) Joanne Schottinger MD, Assistant Medical Director for Quality and Clinical Analysis
We've had patients via the appeals process request proton beam therapy, usually from the Inland Empire where Loma Linda (one of the rare US centers that has this therapy) sits. We have denied in the past as we have appropriate therapeutic options available in plan and to the best of my knowledge, we've been always upheld by the regulators on those.

5.0 REFERENCES:

Aetna CBP 7/2019

1. Aetna considers proton beam radiotherapy (PBRT) medically necessary in *any* of the following radiosensitive tumors:

    1. Chordomas or chondrosarcomas arising at the base of the skull or cervical spine without distant metastases; *or*

    2. Malignancies in children (21 years of age and younger); *or*

    3. Uveal melanomas confined to the globe (i.e., not distant metastases) (the uvea is comprised of the iris, ciliary body, and choroid [the vascular middle coat of the eye]); *or*

    4. Localized unresectable hepatocellular carcinoma (HCC) in the curative setting when documentation is provided that sparing of the surrounding normal tissue cannot be achieved with standard radiation therapy techniques, including intensity-modulated radiation therapy (IMRT), stereotactic body radiation therapy (SBRT), selective internal radiation spheres, and transarterial therapy (for example, chemoembolization).

American Cancer Society – Brooks 2013
In contrast, most studies of proton therapy for prostate cancer suggest that this new approach may be just as good as standard photon radiation treatment at controlling the growth and spread of the cancer, but there is no evidence that proton treatment does a better job of curing the And in spite of the theory that protons cause less damage to normal tissue, there is at present no convincing evidence that urinary (bladder problems), gastrointestinal (rectal leakage or bleeding), or sexual (erectile dysfunction), complication rates are lower following proton therapy. A few studies suggest that rates of some side effects might even be higher…"

United Health Care Coverage Policy- January 2015, 12/2016
Proton beam radiation therapy is proven and medically necessary for treating the following indications:
 Intracranial arteriovenous malformations (AVMs)
 Ocular tumors, including intraocular/uveal melanoma (includes the iris, ciliary body and choroid)
 Skull-based tumors (e.g., chordomas, chondrosarcomas or paranasal sinus tumors)

Proton beam radiation therapy is unproven and not medically necessary for treating ALL other indications, including but not limited to:

- Age-related macular degeneration (AMD)
- Bladder cancer
- Brain and spinal cord tumors
- Choroidal hemangioma
- Esophageal cancer
- Gynecologic cancers
- Head and neck cancers
- Hepatocellular carcinoma
- Lung cancer
- Lymphomas
- Pancreatic cancer
- Prostate cancer
- Vestibular tumors (e.g., acoustic neuroma or vestibular schwannoma)

There is limited clinical evidence that directly compares proton beam therapy (PBT) with other types of radiation therapy. Current published evidence does not allow for any definitive conclusions about the safety and efficacy of proton beam therapy to treat conditions other than those noted above as proven and medically necessary.

Proton beam radiation therapy used in conjunction with intensity-modulated radiation therapy (IMR

A case-matched study of toxicity outcomes after proton therapy and intensity-modulated radiation therapy for prostate cancer.

Fang P, et al. Cancer. 2015.
Show full citation

Abstract

BACKGROUND: The authors assessed whether proton beam therapy (PBT) for prostate cancer (PCa) was associated with differing toxicity compared with intensity-modulated radiation therapy (IMRT) using case-matched analysis.

METHODS: From 2010 to 2012, 394 patients who had localized PCa received 79.2 Gray (Gy) relative biologic effectiveness (RBE) delivered with either PBT (181 patients) or IMRT (213 patients). Patients were case-matched on risk group, age, and prior gastrointestinal (GI) and genitourinary (GU) disorders, resulting in 94 matched pairs. Both exact matching (risk group) and nearest-neighbor matching (age, prior GI/GU disorders) were used. Residual confounding was adjusted for by using multivariable regression. Maximum acute and late GI/GU Common Terminology Criteria for Adverse Events-graded toxicities were compared using univariate and multivariable logistic and Cox regression models, respectively.

CONCLUSIONS: In this matched comparison of prospectively collected toxicity data on patients with PCa who received treatment with contemporary IMRT and PBT techniques and similar dose-fractionation schedules, the

risks of acute and late GI/GU toxicities did not differ significantly after adjustment for confounders and predictive factors.

Neha Vapiwala MD, one of the authors from the study's research team at the University of Pennsylvania, was interviewed for Healio.com, an online news service for journal articles in hematology and oncology. Looking ahead, Dr. Vapiwala explained that these patients will continue to be followed for longer-term side effects, treatment effectiveness, and appearance of secondary cancers related to radiation exposure (e.g. bladder or rectal cancer). Until such long-term data emerges for large numbers of PBT patients, the results of this study show no clear advantage in terms of PBT side effect rates. The conclusions of the authors may bolster the position of private insurance companies that increasingly question whether to cover proton beam treatments.

AUA Update Series 2014:

Since most of the energy of protons is released during the last few mm of their range, known as the Bragg peak, it is associated with less radiation exposure to normal surrounding tissues.53 Early results suggest adequate cancer control rates and a slight improvement in acute toxicity with proton therapy over IMRT, with no difference in late toxicity.54, 55
The enormous cost of setting up a proton center ($150 to $200 million) necessitates careful cost-effectiveness considerations of this new technology.

54. Zietman AL, Bae K, Slater JD et al: Randomized trial comparing conventional-dose with high-dose conformal radiation therapy in early-stage adenocarcinoma of the prostate: long-term results from proton radiation oncology group/american college of radiology 95-09. J Clin Oncol 2010; 28: 1106.

55. Gray PJ, Paly JJ, Yeap BY et al: Patient-reported outcomes after 3-dimensional conformal, intensity-modulated, or proton beam radiotherapy for localized prostate cancer. Cancer 2013; 119: 1729.

Hayes Rating: May 2017

C – For proton beam therapy (PBT) for the treatment of localized prostate cancer.

This Rating reflects the generally positive long-term outcomes obtained with PBT for localized prostate cancer but inadequate evidence concerning the comparative efficacy and safety of PBT relative to other common radiation therapies for this indication.

Uptodate: Radiation Therapy Techniques in Cancer Treatment- September 2020

Proton beam — Proton radiation reduces the dose to normal tissues by allowing for more precise dose delivery because of the unique physical properties of heavy particles. Protons penetrate tissue to a variable

depth, depending upon their energy, and then deposit that energy in the tissue in a sharp peak, known as a Bragg peak (figure 1). This rapid dose falloff at a depth that can be controlled by the initial energy of the protons allows for decreased radiation to adjoining normal tissue by a factor of 2 to 3 [20].

At the present time, the clinical superiority of protons compared with photons is clearly established in some pediatric populations [21,22] and in rare situations when normal structures in close proximity to the treatment target limit the ability to deliver conventional photon beam therapy, such as uveal melanoma [23-25] and sarcomas of the skull base [26,27] and spine [28]. In other situations, such as prostate cancer, proton beams are being increasingly used, but the available data have not demonstrated an advantage compared with other 3D-CRT techniques [29,30]. Although they have been evaluated in a single-arm study in breast cancer [31], as well as randomized trials in esophageal cancer [32] and locally advanced non-small cell lung cancer [33], protons have not yet been established as clinically superior through randomized clinical trials in any adult solid tumor. Additional trials are underway to determine the role of protons. (See "External beam radiation therapy for localized prostate cancer", section on 'Proton beam'.)

MCG- 24rd Ed- Proton Beam Therapy

- Proton beam therapy may be indicated for **1 or more** of the following(1)(2)(3):
  - Gallbladder cancer, and unresectable intrahepatic tumor(60)
  - Head and neck cancer and **ALL** of the following(62)(63):
    - Highly conformal dose distribution required due to close proximity of tissue to critical structures, as indicated by **1 or more** of the following(62):
      - Cavernous sinus invasion
      - Intracranial invasion
      - Orbital invasion
      - Periocular location
      - Perineural invasion
      - Skull base invasion
    - Radiation oncologist note in medical record documents that other radiation therapy techniques (eg, 3-dimensional conformal radiation therapy, intensity modulated radiation therapy) cannot achieve adequate precision.
  - Hepatocellular carcinoma, as indicated by **ALL** of the following(60)(65):

- Intrahepatic tumor
- Patient is not candidate for or refuses surgery and ablation.

- Ocular melanoma and **ALL** of the following(67)(68):
  - No distant metastasis
  - Patient is not candidate for brachytherapy (eg, due to tumor size or location).(71)
- Skull base[A] tumors (eg, chordomas or chondrosarcomas) following surgical resection(74)

Approval

7/17/2015

Rhoda Sharp, MD, MBA
Physician Program Director, Quality Resource Management

Date